Connecting via Winsock to Dialog

Logging in to Dialog

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
****
ENTER PASSWORD:
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Welcome to DIALOG

Dialog level 02.16.02D

Last logoff: 02jul03 18:13:42
Logon file405 03jul03 07:50:48
*** ANNOUNCEMENT ***
***
--File 654 - US published applications from March 15, 2001 to the present are now online. Please see HELP NEWS 654 for details.

***
--File 581 - The 2003 annual reload of Population Demographics is complete. Please see Help News581 for details.

***
--File 156 - The 2003 annual reload of ToxFile is complete. Please see HELP NEWS156 for details.

***
--File 990 - NewsRoom now contains February 2003 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains records from January 2003. The oldest months's records roll out of File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new OneSearch category.
***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
***
***
--SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.
***
--Important news for public and academic libraries. See HELP LIBRARY for more information.
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--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
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NEW FILES RELEASED
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland (File 682)
***
UPDATING RESUMED

***

RELOADED
***Population Demographics -(File 581)
***CLAIMS Citation (Files 220-222)

REMOVED
***

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<
****

* * * * See HELP NEWS 225 for information on new search prefixes and display codes

*** ***

SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
*** DIALOG HOMEBASE(SM) Main Menu ***

Information:
1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:
6. DIALOG(R) Document Delivery
7. Data Star(R)

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
? b 410

03jul03 07:50:49 User268147 Session D102.1
$0.00 0.166 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.00 Estimated cost this search
$0.00 Estimated total session cost 0.166 DialUnits

File 410:Chronolog(R) 1981-2003/Aug
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Set Items Description
--- ----- ----------
? set hi %%%;set hi %%%
HILIGHT set on as "
HILIGHT set on as "
? b 5, 34, 155, 172
03jul03 07:50:57 User268147 Session D102.2
$0.00 0.073 DialUnits File410
$0.00 Estimated cost File410
$0.03 TELNET
$0.03 Estimated cost this search

$0.03 Estimated total session cost 0.239 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2003/Jun W5
(c) 2003 BIOSIS
File 34:SciSearch(R) Cited Ref Sci 1990-2003/Jun W5
(c) 2003 Inst for Sci Info
File 155:MEDLINE(R) 1966-2003/Jun W5
(c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have changed. Please see HELP NEWS 155.
File 172:EMBASE Alert 2003/Jun W5
(c) 2003 Elsevier Science B.V.

Set Items Description
--- ----- ---------
? s "epidermolysis bullosa"
S1 1899 "EPIDERMOLYSIS BULLOSA"
? s cytosine
S2 48142 CYTOSINE
? s s1 and s2
1899 S1
48142 S2
S3 2 S1 AND S2
? type s3/full/all

3/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

08474655 BIOSIS NO.: 199344024655
PCR-based detection of two exonic polymorphisms in the human type VII collagen gene (COL7A1) at 3p21.1.
AUTHOR: Christiano Angela M(a); Chung-Honet Linda C; Hovnanian Alain; Uitto Jouni
AUTHOR ADDRESS: (a)Dep. Dermatol., Jefferson Med. College, Thomas Jefferson University, Philadelphia, Pa. 19107
JOURNAL: Genomics 14 (3):p827-828 1992
ISSN: 0888-7543
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 81295-04-7: ALUI; 73-40-5Q: GUANINE; 69257-39-2Q: GUANINE ; 73-24-5: ADENINE; 71-30-7: CYTOSINE; 60-18-4: TYROSINE
DESCRIPTORS:
MAJOR CONCEPTS: Anthropology; Biochemistry and Molecular Biophysics; Clinical Chemistry (Allied Medical Sciences); Dermatology (Human Medicine, Medical Sciences); Genetics; Pathology; Population Genetics (Population Studies)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Hominidae (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
CHEMICALS & BIOCHEMICALS: ALUI; GUANINE; ADENINE; CYTOSINE; TYROSINE
GEOGRAPHICAL NAME: USA (North America, Nearctic region)
MISCELLANEOUS TERMS: ALLELIC FREQUENCY; ALUI POLYMORPHISM; CAUCASIAN; CO-SEGREGATION; COMPLEMENTARY DNA; CYTOSINE TO TYROSINE TRANSITION; DIAGNOSTIC METHOD; EPIDERMOLYSIS BULLOSA; FINNS; GENE MAPPING; GENE MARKER; GREEKS; GUANINE TO ADENINE TRANSITION; JAPANESE; MENDELIAN SEGREGATION; MOLECULAR DIAGNOSTICS; NOTE; POLYMERASE CHAIN

FINE JD, 2000, V42, P1051, J AM ACAD DERMATOL
FINE JD, 1991, V24, P119, J AM ACAD DERMATOL
FRAME SR, 1988, V193, P1420, J AM VET MED ASSOC
GOUREAU JM, 1989, V62, P345, B ACAD VET FR
HOOD J, 2001, V11, P463, TRENDS CELL BIOL
JOHNSON GC, 1998, V99, P329, J COMP PATHOL
KOHN CW, 1989, V21, P297, EQUINE VET J
KORGE BP, 1996, V74, P59, J MOL MED-JMM
LYKKEANDERSEN J, 2001, V293, P1836, SCIENCE
NAGY E, 1998, V23, P198, TRENDS BIOCHEM SCI
OLIVRY T, 1999, V36, P616, VET PATHOL
PALAZZI X, 2000, V115, P135, J INVEST DERMATOL
PULKKINEN L, 1999, V18, P29, MATRIX BIOL
SPIRITO F, 2002, V3, P684, J INVEST DERMATOL
TERWILLIGER JD, 1995, V56, P777, AM J HUM GENET

? s s2 and laminin?
48142 S2
41121 LAMININ?
S4 27 S2 AND LAMININ?
? type s4/full/all

4/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14140812 BIOSIS NO.: 200300134841
Delayed dedifferentiation and retention of properties in dissociated adult skeletal muscle fibers in vitro.
AUTHOR: Brown L D; Schneider M F(a)
AUTHOR ADDRESS: (a)Department of Biochemistry and Molecular Biology, School of Medicine, University of Maryland, 108 N. Greene Street, Baltimore, MD, 21201, USA**USA E-Mail: mschneid@umaryland.edu
JOURNAL: In Vitro Cellular & Developmental Biology Animal 38 (7):p411-422 July-August 2002 2002
MEDIUM: print
ISSN: 1071-2690
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Adult skeletal muscle fibers can be isolated and cultured but tend to dedifferentiate and sprout with time in culture. We examined isolated adult mouse flexor digitorum brevis muscle fibers under various culture conditions by monitoring maintenance of the same fibers at 2-d intervals using survival analysis. Fibers plated on laminin and cultured in serum-free media did not show sprouting and exhibited significantly (P<0.0001) longer survival (median survival time, T50=10.2 d) than fibers in serum-containing media (T50=3.3 d). Cell proliferation was markedly suppressed in serum-free cultures. Multiple or delayed Ca2+ transients in response to brief field stimulation were often observed in dedifferentiated fibers after several d in serum-containing media but were not observed in fibers in serum-free media. The addition of cytosine arabinoside to serum-containing cultures did not prolong fiber survival (P=0.39) and did not eliminate sprouting but did greatly suppress proliferation of nonmuscle cells. Fibers cultured in agarose gel with serum exhibited small, bud-like extensions but no sprouts and did not survive as long (T50=6.2 d) as fibers plated on laminin and cultured in serum-free media (T50=10.2 d) did. These results demonstrate that both morphological and physiological properties of fibers become modified in serum-containing media but can be retained by culturing without serum.

REGISTRY NUMBERS: 14127-61-8: CALCIUM(II) ION; 147-94-4: CYTOSINE ARABINOSIDE
DESCRIPTORS:
MAJOR CONCEPTS: Methods and Techniques; Muscular System (Movement and Support)
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: mouse (Muridae)--adult, animal model
ORGANISMS: PARTS ETC: flexor digitorum brevis muscle--muscular system; muscle cells--muscular system, proliferation; skeletal muscle fibers--dedifferentiation, morphological properties, muscular system, physiological properties, sprouting
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: agarose gel; calcium(II) ion; cytosine arabinoside; laminin
METHODS & EQUIPMENT: cell culture--culturing techniques, laboratory techniques
MISCELLANEOUS TERMS: cell survival; serum-containing media--culture medium; serum-free media--culture medium
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10069 Biochemical Studies-Minerals
17504 Muscle-Physiology and Biochemistry
32500 Tissue Culture, Apparatus, Methods and Media
BIOSYSTEMATIC CODES:
86375 Muridae

4/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11586488 BIOSIS NO.: 199800367184
The extracellular matrix molecule, laminin, induces Purkinje cell dendritic spine proliferation in granule cell depleted cerebellar cultures.
AUTHOR: Seil Fredrick J(a)
AUTHOR ADDRESS: (a)Neurol. Res., VA Med. Cent., Portland, OR 97201**USA
JOURNAL: Brain Research 795 (1-2):p112-120 June 8, 1998
ISSN: 0006-8993
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Granule cells and glia were eliminated or reduced in organotypic cerebellar cultures exposed to cytosine arabinoside.
Transplantation of such granuloprival cultures with glia or exposure to astrocyte conditioned medium in the absence of parallel fibers (granule cell axons) resulted in proliferation of Purkinje cell dendritic spines.
The aim of the present study was to identify specific astrocyte secreted factors that induced dendritic spine proliferation. Known astrocyte secreted, neurite promoting factors were screened by application to granuloprival cultures and assayed for dendritic spine proliferation by electron microscopy. An extracellular matrix molecule, laminin, evoked sprouting of Purkinje cell dendritic spines. Dendritic spine proliferation was not associated with known neurite promoting parts of the laminin molecule, as two laminin-derived peptides with identified neurite promoting domains did not induce dendritic spine sprouting. The purpose of laminin-induced dendritic spine

S3 2 S1 AND S2
S4 27 S2 AND LAMININ?
S5 13 AU='MILENKOVIC D J' OR AU='MILENKOVIC D Z' OR AU='MILENKOVIC DJ' OR AU='MILENKOVIC DRAGAN' OR AU='MILENKOVIC DZ'
S6 110 AU='CHAFFAUX S' OR AU='CHAFFAUX S T' OR AU='CHAFFAUX SAINT' OR AU='CHAFFAUX STEPHANE'
S7 28 AU='TAOURIT S' OR AU='TAOURIT SEAD'
S8 318 AU='GUERIN G' OR AU='GUERIN G F' OR AU='GUERIN G J' OR AU='GUERIN G R' OR AU='GUERIN G.' OR AU='GUERIN GERARD' OR AU='GUERIN GF' OR AU='GUERIN GILLES' OR AU='GUERIN GLENN' OR AU='GUERIN GLENN F' OR AU='GUERIN GUY'
S9 34 AU='GUERIN G J' OR AU='GUERIN G R' OR AU='GUERIN G.' OR AU='GUERIN GERARD'
S10 451 S5 OR S6 OR S7 OR S8
S11 2 S10 AND (S1 OR S2 OR LAMININ?)
S12 3 S11 OR S3

[redacted]

STIC-ILL

RL1.J8
Adams

From: STIC-Biotech/ChemLib
Sent: Thursday, July 03, 2003 1:08 PM
To: STIC-ILL
Subject: FW: 10/053662

-----Original Message-----
From: Mayes, Laurie
Sent: Thursday, July 03, 2003 9:14 AM
T : STIC-Biotech/ChemLib
Subject: 10/053662

Please send me a copy of the following:

PCR-based detection of two exonic polymorphisms in the human type VII collagen gene (COL7A1) at 3p21.1.
AUTHOR: Christiano Angela M(a); Chung-Honet Linda C; Hovnanian Alain; Uitto Jouni
JOURNAL: Genomics 14 (3):p827-828 1992

Animal models for skin blistering conditions: absence of laminin 5 causes hereditary junctional mechanobullous disease in the Belgian horse.
Spirito Flavia; Charlesworth Alexandra; Linder Keith; Ortonne Jean-Paul; Baird John; Meneguzzi Guerrino
Journal of investigative dermatology (United States) Sep 2002, 119 (3) p684-91,

---

Corrective gene transfer of non-Herlitz junctional epidermolysis bullosa keratinocytes.
AUTHOR: Keane F M(a); McGrath J A(a); Eady R A J(a); Pommeret O; Ortonne J P; Meneguzzi G; Vailly J
JOURNAL: Journal of Investigative Dermatology 114 (4):p868 April, 2000
CONFERENCE/MEETING: 61st Annual Meeting of the Society for Investigative Dermatology. Chicago, Illinois, USA May 10-14, 2000

Thank you,

Laurie Mayes; AU 1653; 605-1208
CM1 10A16; MAILBOX CM1 9b01

723

Splicing Defects in the PTEN Gene Leading to Exon Skipping or Intron Inclusion

J.T. Celebi, M. Wanner, X.L. Ping, and M. Peacocke
Columbia University, New York, New York

PTEN is the susceptibility gene for two autosomal dominantly inherited hamartoma syndromes, Cowden syndrome (CS) and Bannayan–Zonana syndrome (BZS). PTEN tumor suppressor gene encodes a dual-specificity phosphatase. It contains nine exons, in which the core phosphatase domain resides in exon 5. A variety of germline mutations have been identified in PTEN including missense, nonsense, frameshift, and splice-site mutations. To date, 11 splice site mutations in PTEN have been reported, however, in general, the splicing defects in PTEN have not been studied in detail. In this study, we identified three novel splice site mutations in PTEN, in two kindreds with CS and one individual with BZS phenotype. Additionally, we analyzed the transcripts by RT-PCR using RNA obtained from EBV-transformed lymphoblastoid cell lines. The 1.2 kb PTEN c-DNA was subcloned into a pCR 2.1 plasmid vector and sequenced. The IVS3, 3′ splice acceptor site mutation (210–1 GA), resulted in out-of-frame skipping of entire exon 4 (44 nucleotides) and led to a premature termination codon. The IVS4 and IVS7, 5′ splice donor site mutations (253+2 TC and 801+1 GA), resulted in partial inclusion of the intronic sequences by using cryptic donor sites in the downstream intron (4 and 75 nucleotides, respectively). Both resulted in premature stop codon signals. Thus, these products would be subject to nonsense mediated decay. These results provide further evidence of splicing defects in PTEN in individuals with CS and BZS.

724

Individuals with Genetic Predisposition to Uveal Melanoma do not Harbor Mutations in the Coding Regions of either P16INKA, P14ARF or CDK4 Genes

N. Soufir, L. Desjardins, C. Levy, P. Schlienger, J. Bombled, B. Bressac-Paillerets, and D. Stoppa-Lyonnet
Inst. Recherche Sur le Peau. Pavillion Bazin; Paris, France

In familial cutaneous malignant melanoma (CMM), disruption of the retinoblastoma (Rb) pathway frequently occurs through inactivating mutations in the *p16Inka/Cdkn2/Mts1* gene or activating mutations in the G1-specific cyclin dependent kinase 4 gene (*Cdk4*). Uveal malignant melanoma (UMM) also occurs in a familial setting, or sometimes in association with familial and sporadic CMM. Molecular studies of sporadic UMM have revealed deletions covering the *INKA-ARF* locus (encoding p16INKA and p14ARF) in a large proportion of tumours. We hypothesised that germ-line mutations in the *p16Ink4a, p14arf*, or *Cdk4* genes might contribute to some cases of familial UMM, or to some cases of UMM associated with another melanoma. Out of 155 patients treated at the Institut Curie for UMM between 1994 and 1997, and interviewed about their personal and familial history of melanoma, we identified seven patients with a relative affected with UMM (n = 6) or CMM (n = 1), and two patients who have had, in addition to UMM, a personal history of second melanoma, UMM (n = 1), or CMM (n = 1). We screened by PCR-SSCP the entire coding sequence of the *INKA-ARF* locus (exon 1α from *p16inka*, exon 1β from *p14arf*, and exons 2 and 3, common to both genes), as well as the exons 2, 5, and 8 of the *Cdk4* gene, coding for the functional domains involved in p16 and/or cyclin D1 binding. A previously reported polymorphism in exon 3 of the *INKA-ARF* locus was found in one patient affected with bilateral UMM, but no germ-line mutations were detected, either in *p16Inka, p14arf* or *Cdk4* genes. Our data support the involvement of other genes in predisposition to uveal melanoma.

725

Corrective Gene Transfer of Non-Herlitz Junctional Epidermolysis Bullosa Keratinocytes

F.M. Keane, J.A. McGrath, R.A.J. Eady, O. Pommeret,* J.P. Ortonne,* G. Meneguzzi,* and J. Vailly*
*St John's Institute of Dermatology, London, U.K.; *U385 Inserm, Faculte de Medecine, Nice, France*

The junctional types of epidermolysis bullosa (JEB) are characterised by skin fragility and blistering. In Herlitz JEB, there is absent laminin 5 consequent to homozygous premature termination codon mutations in one of the three laminin 5 genes. In contrast, non-Herlitz JEB (NHJEB) results from less disruptive mutations of the laminin 5 or collagen XVII genes causing reduced levels of the affected protein. Patients have significant disability but a normal life expectancy. Somatic gene therapy therefore, is a worthwhile goal. Our aim was to induce the phenotypic reversion of NHJEB keratinocytes deficient in the β3 chain of laminin 5 by transfer of a *myc*-tagged laminin β3 transgene.

NHJEB keratinocytes were cultured by standard methods from a shave biopsy of the right upper arm of a patient with known compound heterozygous mutations in the LAMB3 gene (R42X,E210K). Keratinocytes were incubated with a pLXSN retroviral construct carrying a *myc*-tagged laminin β3 transgene or with the retroviral vector alone to act as control. Immunofluorescence using mAb GB3 which binds native laminin 5, and a polyclonal antibody to β3B which is specific for β3 chain of laminin 5 showed increased positivity in transduced *versus* control keratinocytes. Immunoprecipitation studies confirmed increased production of β3 chain of laminin 5 in reverted keratinocytes compared to controls as well as evidence of assembly of trimeric laminin 5. Preliminary adhesion assays showed increased adhesive ability of transduced compared to control keratinocytes.

This initial data showing phenotypic reversion of NHJEB keratinocytes has encouraged us to undertake a more comprehensive assessment of the genetically manipulated cells.

726

Cutaneous Granuloma Formation in a Murine Model of X-Linked Chronic Granulomatous Disease

J. Petersen, T.S. Hiran, A.F. Hood, J.B. Travers, and M.C. Dinauer
Indiana University, Indianapolis, Indiana

As a result of the inability of their phagocytes to undergo a respiratory burst, patients with the genetic condition chronic granulomatous disease (CGD) develop recurrent infections with catalase-positive bacterial and fungal pathogens, and are predisposed to chronic inflammatory granulomatous lesions in many organs including the skin. Previously, our laboratory has generated a murine model of X-linked CGD by homologous recombinant deletion of the gp91phox component of the NADPH oxidase. Functional studies with these X-CGD mice demonstrated increased numbers of alveolar exudate neutrophils in response to intratracheal administration of sterile *Aspergillus fumigatus* (AF) hyphae, in comparison to wild-type mice (*J Exp Med* 185:207, 1997). In our present study, sterile AF hyphae or PBS vehicle were injected into the ears of X-CGD and wild-type control mice. Inflammation was assessed by obtaining 5 mm punch biopsies of the injection sites at various times (1–30 d) following injection for weighing and measurement of ear thickness, as well as histologic evaluation. Intradermal injection of AF (but not PBS alone) resulted in a significant ($p < 0.05$, ANOVA) inflammatory response in X-CGD mice by 24 h, with formation of neutrophil-rich granulomas within one week. However, wild-type mice did not exhibit inflammation or granuloma formation over a 30 d period in response to intradermal AF. These studies describe a model system for cutaneous granuloma formation, as well as a clinical functional test for CGD in this murine model system, which is currently being used in developing CGD gene therapy protocols.

727

The Expression and Distribution of Major Desmosome Components is Altered in Striate Palmoplantar Keratoderma

H. Wan, J.R. McMillan, F. Keane, N.V. Whittock, R.S. Buxton,* D.K.B. Armstrong,† J.A. McGrath, and R.A. Eady
*St John's Institute of Dermatology, GKT School of Medicine, St Thomas' Hospital, London, U.K.; *NIMR, Mill Hill, London, U.K.; †Department of Medical Genetics, Queens University of Belfast, Belfast, U.K.*

Striate palmoplantar keratoderma (SPPK), an autosomal dominant disorder, may be associated with haploinsufficiency of desmoplakin I (DpI) or desmoglein 1 (Dsg1). This study aimed to analyze the expression and distribution patterns of major desmosome (DM) proteins in palm skin from normal individuals and from two patients affected with SPPK. Dual labeling on skin sections was carried out using antibodies to DpI/II, the Dsg isoforms, plakoglobin (Pg) and plakophilin 1 (Pkp1) and examined by laser scanning confocal microscopy. In normal palm epidermis, Dp and Dsg were the most abundant DM antigens, being colocalized to the periphery of the lower and mid-spinous cells. However, in the upper spinous layer the localization of these proteins was partly disassociated with Dsg expression occurring intracellularly. Dp expression was consistently higher than that of Dsg in the basal and granular layers but was almost absent in the cornified layer. The expression of Pg and Pkp1 was much lower than that of Dp. In the patient with a Dsg 1 mutation, staining for Dsg, Pg and Pkp1 was generally very weak, although Dp staining was normal. The peripheral linear staining for Pkp1 and Pg was disrupted. EM showed small DMs and attenuation of midline structures. In the patient with a Dp mutation Dp and Dsg staining was disrupted, and the DMs were ultrastructurally small. The preferential involvement of the palms and soles in SPPK should be considered in the light of the complex organization of DMs occurring in different layers of normal ridged epidermis.

728

Mutation Detection in Epidermolysis Bullosa in a Global Population by the DebRA Molecular Diagnostics Laboratory at Jefferson

E. Pfendner, A. Nakano, K. Nielsen, L. Pulkkinen, and J. Uitto
Thomas Jefferson University, Philadelphia, Pennsylvania

Epidermolysis Bullosa (EB) is a group of heritable blistering disorders marked by separation of layers within the cutaneous basement membrane zone either below the lamina densa (dystrophic EB, DEB), within the lamina lucida (junctional EB, JEB) or within the basal keratinocytes (EB simplex). Molecular diagnosis for DEB and JEB has been performed for an International referral base. As of today, 150 DEB and 130 JEB samples have been submitted which meet the diagnostic criteria for analysis. Using heteroduplex scanning of PCR products, followed by nucleotide sequencing, the overall mutation detection rate was 54% for DEB and 85% for JEB. DEB mutations have been detected in the COL7A1 gene in five categories: splice junctions (20.8%), missense (4.8%), nonsense (15.2%), insertion/deletion (33.6%), and glycine substitutions (25.6%). JEB mutations have been identified in six different genes: LAMA3, LAMB3, and LAMC2 of laminin 5; ITGA6 and ITGB4 of alpha 6/beta 4 integrin; and BPAG2 for the 180-kDa bullous pemphigoid antigen. JEB mutations were identified in splice junction (12.5%), missense (20.8%), nonsense (33.3%), and insertion/deletion (33.3%) categories. R.635X in LAMB3 was the predominant JEB mutation comprising 45.8% of all LAMB3 mutations and 25% of all JEB mutations. These molecular analyses lead to prenatal diagnosis for 61 pregnancies, 40 DEB and 21 JEB. Linkage analysis was used for prenatal diagnosis in another 10 DEB families. In 65 pregnancies genotype was correctly predicted while six pregnancies are ongoing. These results indicate that DNA based prenatal testing for recurrence of EB is accurate, expedient and reliable.